July 23, 1999

VETERINARY SERVICES MEMORANDUM NO. 800.85

Subject: Avian Influenza Vaccines

To: Biologics Licensees, Permittees, and Applicants
Directors, Center for Veterinary Biologics
Director, National Veterinary Services Laboratories

I. PURPOSE

This memorandum informs all interested parties of the conditions under which the Center for Veterinary Biologics will consider license applications for Avian Influenza Vaccines. This information supplements the applicable Standard Requirements found in 9 CFR 113.200 and 113.300.

II. CANCELLATION

This memorandum cancels Veterinary Biologics Memorandum No. 800.85 dated July 6, 1995.

III. BACKGROUND

USDA, APHIS, Veterinary Services (VS) considers avian influenza (AI) in chickens to be an exotic disease and regulates the importation or interstate movement of AI viruses by permit (9 CFR 122.2). This policy is clarified and updated in VS memorandum No. 565.12.

IV. PRODUCT MASTER SEED VIRUSES (MSVs)

Licensees and applicants (firms) must meet all applicable Standard Requirements for MSVs, including but not limited to 9 CFR 113.200 and 113.300, with the following additional considerations:

A. Interstate Movements

VS will continue to regulate all importations or interstate movements of AI viruses by permit, under 9 CFR 122.2.

B. Conventional Killed Vaccines

APHIS will consider licensing conventional killed AI vaccines provided that firms obtain and use the MSVs under the following conditions:

1. *Acceptable MSVs* - Firms must only use AI viruses of low pathogenicity obtained from the Diagnostic Virology Laboratory of the National Veterinary Services Laboratories (NVSL), as MSVs for conventional killed vaccines. Firms may obtain any hemagglutinin (H) type from this source.

2. *VS Permit Required* - Firms must obtain a permit from VS to obtain such isolates. VS will issue permits for AI isolates with the restriction that the virus be used only for *in vitro* studies. Furthermore, VS may require a facility inspection before issuing such a permit. AI isolates may be used for the production and testing of vaccine only when authorized by CVB.

3. *State Authorization Required* - Firms must also obtain written authorization from the appropriate State officials for receipt and use of such isolates.

C. Recombinant Derived Vaccines

APHIS will consider licensing live or inactivated recombinant vaccines, subunit vaccines, or other biotechnology-derived AI vaccines produced from recombinant-derived MSVs. Firms must obtain a VS permit to acquire the AI viruses necessary to construct such MSVs.

D. Conventional Modified Live Vaccines

Due to the high rate of mutation documented for AI viruses, APHIS will not consider license applications for conventional modified live AI vaccines.

V. PRODUCT DEVELOPMENT

All applicable Standard Requirements for licensure must be met, including but not limited to 9 CFR 113.200 and 113.300, with the following additional considerations:

A. Product Claims

Firms may develop products with a claim for use in either chickens or turkeys for any H type. Firms must support all claims for each species, each H type, and each age and route of administration with appropriate data.

B. Challenge Studies

Firms must support applications for regularly licensed products with appropriate vaccination-challenge efficacy data. Firms must conduct these challenge studies under biosafety level 3 (BL3) containment conditions. Prior to the initiation of such a study, the firm must obtain APHIS approval of the laboratory, study protocol, and challenge virus to be used.

C. Conditional Licensing

APHIS will only consider applications for conditionally licensed products if the conditions found in 9 CFR 102.6 are met. Furthermore, all applicants or licensees seeking or holding conditional licenses for AI vaccines must work toward eventual regular licensure of these products.

VI. PRODUCT LICENSE RESTRICTIONS

A. General License Restrictions

APHIS will add the following restrictions to all licenses issued for AI vaccines:

1. *Distribution in Each State* - "Distribution in each State shall be limited to authorized recipients designated by proper State officials--under such additional conditions as these authorities may require."

2. *Distribution for Export* - "Export distribution shall be limited to authorized recipients designated by proper animal health regulatory officials-- under such additional conditions as these authorities may require."

B. Additional License Restrictions

APHIS will add the following additional restrictions to licenses issued for all AI vaccines for use in chickens, as well as for all H5 and H7 AI vaccines for use in turkeys: "Domestic distribution and use shall be under the supervision or control of USDA, APHIS, Veterinary Services, as part of an official USDA animal disease control program."

VII. PRODUCT LABELING

A. Limited Species Recommendations

Because of the license restrictions on distribution and use, individual product labels may recommend use of the product in chickens or turkeys but not both.

B. Distribution Statement

For licenses carrying the restriction listed in VI., B. above, the domestic product labels must carry the following statement: "This product may only be distributed and used as part of an official USDA animal disease control program."

C. Indication of H Type

Product labels must indicate the H type of the AI virus used to produce the product.

/s/ Thomas E. Walton for

Alfonso Torres
Deputy Administrator
Veterinary Services